10 is increased so that all numbers, letters, and reference characters are at least 0.32 cm. No new matter is introduced. Applicants believe that these amendments overcome the objections to the drawings.

CLAIM REJECTIONS UNDER 35 U.S.C. §103

Claims 1-4, 13-19, and 23-26 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ekins *et al.*, EP 304,202, ('202 patent) in view of Ekins *et al.*, J. of Clinical Immunoassay, (Immunoassay reference). This rejection is respectfully traversed.

The present invention relates to a microscale binding assay, an analyte binding array and a kit for use in a binding assay with a high sensitivity for very low quantities of analyte. All three independent claims of the instant invention, 1, 23, and 26, require the analyte binding partner to be present in the sorbent zone in excess relative to the analyte, so that "any analyte present in the defined volume is substantially depleted from the sample" (emphasis added). As explained on page 14, lines 17-22, of the instant specification, "substantially depleted" means that "at least about 60% of the analyte will be captured by a high affinity binding partner having a $K_A > 10^{10}$ liter mole $^{-1}$" (emphasis added).

The '202 patent is directed to the determination of ambient analyte concentrations in liquids. The reference teaches that "only an insignificant proportion of any analyte present in the liquid sample becomes bound to the binding agent" (claim 1, emphasis added). The Examiner acknowledged that the reference does not teach the analyte being substantially depleted from the sample, but relied on the Immunoassay reference for teaching this limitation. Applicants respectfully disagree with the Examiner's reading of the Immunoassay reference.

The Immunoassay reference teaches ambient analyte immunoassay. In the ambient analyte immunoassay, the proportion of bound analyte molecules is small and "the resulting reduction in the ambient analyte concentration may be ignored" (page 173, left column, emphasis added). This "ignored" amount of the analyte depleted from the sample is further defined as "less than 1%" by the reference (page 173, left column). Thus, the Immunoassay reference does not teach or suggest the analyte being substantially depleted from the sample. Moreover, the reference teaches away from the present invention by requiring that only an insignificant amount of the analyte (less than 1%) is depleted from the sample. In view of this teaching, one skilled in the art would not

have been motivated to arrive at the present invention, which requires a substantial depletion of the analyte from a sample. In light of the foregoing, applicants respectfully submit that the '202 patent and the Immunoassay reference, either alone or in combination, cannot make claims 1, 23, and 26 obvious. Claims 2-4, 13-19, 24, and 25 depend, directly or indirectly, on claims 1, 23, and 26 and are not obvious for at least the same reasons.

Claims 1-4, 13-19, 21, and 23-26 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the '202 patent in view of Ekins *et al.*, Analytica Chimica Acta (Analytica reference). The Examiner's argument based on the '202 patent and the Analytica reference, is substantially the same as that based on the '202 patent and the Immunoassay reference, and suffers from the same defects. The Examiner relied on the Analytica reference for teaching the analyte being substantially depleted from the sample. Applicants respectfully disagree with the Examiner's reading of the Analytica reference.

Similarly to the Immunoassay reference, the Analytica reference discloses ambient analyte immunoassay. It is required by the method, that the proportion of bound analyte be so small that the "disturbance to the ambient analyte concentration can be ignored" (page 80, first paragraph). This "ignored" amount of the analyte depleted from the sample is further defined as "invariably less than 1% regardless of the analyte concentration" by the reference (page 80, first paragraph, last sentence). Therefore, like the Immunoassay reference, the Analytica reference does not teach or suggest the analyte being substantially depleted from the sample. Instead, the Analytica reference teaches away from the present invention by requiring that only an insignificant amount of the analyte (less than 1%) is depleted from the sample. In light of the foregoing, applicants respectfully submit that the '202 patent and the Analytica reference, either alone or in combination, cannot make claims 1, 23, and 26 obvious. Claims 2-4, 13-19, 24, and 25 depend, directly or indirectly, on claims 1, 23, and 26 and are not obvious for at least the same reasons.

Claims 5-10 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the '202 patent, and either Immunoassay reference or Analytica reference, in further view of Ullman *et al* (U.S. Patent 5,512,659). Claim 11 is rejected under 35 U.S.C. § 103(a) as unpatentable over the '202 patent, and either Immunoassay reference or Analytica reference in further view of Waggoner *et al*. (U.S. Patent 5,368,486). Claim 12 is rejected under 35 U.S.C. § 103(a) as being unpatentable over the '202 patent, and either Immunoassay reference or Analytica reference in

view of the Waggoner *et al.*, in further view of Lee *et al.* (U.S. Patent 5,453,505). Claim 20 is rejected under 35 U.S.C. § 103(a) as being unpatentable over the '202 patent, and either Immunoassay reference or Analytica reference in view of Northrup *et al.* (U.S. Patent 5,639,423). Applicants respectfully traverse these rejections.

As discussed above, the '202 patent, the Immunoassay reference, and the Analytica reference, either alone or in combination, cannot make the base claim 1 obvious, because they teach away from the binding assay of the present application, which requires the analyte to be substantially depleted from the sample. Claims 5-10, 11, 12, and 20 depend directly or indirectly from claim 1 and cannot be made obvious by the '202 patent, Immunoassay reference, and Analytica reference for at least the same reasons.

Ulman *et al.*, Waggoner *et al.*, Lee *et al.*, and Northrup *et al.* cannot remedy the defect of the '202 patent, the Immunoassay reference, and the Analytica reference, and are not relied upon by the Examiner for such. Ulman *et al.*, Waggoner *et al.*, Lee *et al.*, and Northrup *et al.* have no teaching whatsoever of a binding assay utilizing a plurality of sorbent zones containing an analyte binding partner, let alone a binding assay, which requires an excess of the analyte binding partner "relative to the analyte, so that any analyte present ... is substantially depleted from the sample." Therefore, none of the cited references, either alone or in combination, can motivate one skilled in the art to arrive at claims 5-10, 11, 12, and 20. The rejection is improper and should be withdrawn.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Fullerton, California, telephone number 714-773-6969 to discuss the steps necessary for placing the application in condition for allowance.

Respectfully submitted,

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